Claims

1. A transcriptional activator comprising:

a DNA binding moiety; and

a peptide approximately 6-25 amino acids in length, which peptide is covalently attached to the DNA binding domain and does not correspond to a fragment of a naturally-occurring transcriptional activator.

2. The transcriptional activator of claim 1, wherein the peptide is approximately 8-17 amino acids in length.

3. The transcriptional activator of claim 2, wherein the peptide is 6, 8, 11, or 13 amino acids in length.

4. A transcriptional activator comprising:

a DNA binding moiety; and

a substantially hydrophobic polypeptide between about 6 and 25 amino acids in length, which peptide is linked to the DNA binding moiety in a manner that does not interfere with its DNA binding activity,

the transcriptional activator being characterized by an ability, when expressed in yeast cells, to activate transcription from a promoter including a recognition site for the DNA binding moiety approximately 250-1000 basepairs upstream of the transcription start site.

5. The transcriptional activator of claim 4, which transcriptional activator, when expressed in yeast, does not squelch transcriptional activation by LexA-Gal4.

6. The transcriptional activator of claim 5, which transcriptional activator, when expressed in yeast, does not squelch transcriptional activation by LexA-Gal11.

7. The transcriptional activator of claim 4 or claim 5, in which the DNA binding moiety comprises Gal4(1-100) and the activator, when expressed in yeast, activates transcription at least half as well as does Gal4 from a promoter containing at least one Gal4 DNA binding site approximately 250-1000 basepairs upstream of the transcription start site.

8. The transcriptional activator of claim 1 or claim 4 wherein the peptide includes at least one aromatic amino acid.

9. The transcriptional activator of claim 1 or claim 4, wherein the peptide does not include any basic amino acids.

10. The transcriptional activator of claim 1 and claim 4, wherein the peptide is selected from the group consisting of LS4 (QLPPWL); LS8 (QFLDAL); LS11 (LDSFYV); LS12 (PPPPWP); LS17 (SWFDVE); LS19 (QLPDLF); LS20 (PLPDLF); LS21 (FESDDI); LS24 (QYDLFP); LS25 (LPDLIL); LS30 (LPDFDP); LS35 (LFPYSL); LS51 (FDPFNQ); LS64 (DFDVLL); LS102 (HPPPPI); LS105 (LPGCFF); LS106 (QYDLFD); LS120 (YPPPPF); LS123 (PLPPFL); LS135 (LPPPWL); LS136 (VWPPAV); LS152 (DPPWYL); LS153 (LY); LS158 (FDPFGL); LS160 (PPSVNL); LS201 (YLLPTCIP); LS202 (LQVHNST); LS203 (VLDFTPFL); LS206 (HHAFYEIP); LS212 (PWYPTPYL); LS223 (YLLPFLPY); LS225 (YFLPLLST); LS232 (FSPTFWAF); LS241 (LIMNWPTY), each of these peptides extended by Gal4 residues 96-100, and each of these peptides extended by residues corresponding to Gal4 96-100 except that one or both of Gal4 residues 99 and 100 has been substituted with a different amino acid.

11. A method of identifying novel transcriptional activators, the method comprising steps of:

providing a collection of synthetic oligonucleotides of random sequence, which oligonucleotides are approximately 18-24 base pairs in length;

linking oligonucleotides from the collection to a nucleic acid encoding a polypeptide with DNA binding activity, thereby producing a library of artificial transcriptional activator genes;

expressing encoded hybrid proteins from the library of artificial transcriptional activator genes; and

identifying hybrid proteins that activate transcription.

12. The method of claim 11 further comprising a step of identifying hybrid proteins that, when expressed in yeast cells, do not squelch transcriptional activation by Gal4.

13. A method of activating transcription in a cell, the method comprising:

providing to the cell a transcriptional activator of claim 1 or claim 4 under conditions that the transcriptional activator will bind to a DNA site in the cell and activate transcription; and

identifying those transcriptional activators that:

i) stimulate transcription at least half as effectively as does a known transcriptional activator linked to the same DNA binding moiety and assayed on the same reporter gene; and

ii) do not squelch transcriptional activation by acidic activators in yeast.

14. In a di-hybrid protein-protein interaction assay the improvement that comprises utilizing Gal11 as a transcriptional activation domain.

15. A method of identifying protein-protein interactions, the method comprising:

providing a first fusion comprising a DNA binding domain fused to a library of DNA fragments;

providing a second fusion comprising a target protein fused to a polypeptide comprising a region of Gal4 with which Gal11P interacts;

introducing the first and second fusion in a cell including Gal11P; and

identifying library members that interact with the target protein by identifying those cells in which transcription is activated.

16. An isolated protein that is a derivative of TBP, which derivative is selected from the group consisting of TBP N69R and TBP V71R.

17. A method of altering transcriptional activation, comprising:

introducing into a cell a TBP derivative selected from the group consisting of TBP N69R and TBP V71R.